Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Safety profile of hydroxychloroquine and azithromycin combined treatment in COVID-19 patients ☆

We agree with colleagues that the hydroxychloroquine-azythromycin (HCQ-AZ) combination may potentially lead to drug-drug interactions [1]. Given that both drugs are known to have potential cardiotoxicity, we paid a rigorous attention to avoiding HCQ-AZ in patients with cardiac diseases, abnormal EKG, dyskalemia or the routine use of other interacting medications. The systematic pre-therapy workup included serum electrolyte analysis, and an electrocardiogram with corrected QT measurement (Bazett's formula). Close serum electrolyte analysis monitoring was performed in patients with low serum potassium levels at baseline. An electrocardiogram was routinely performed 48 hours after the start of treatment. Treatment with HCQ was discontinued when the corrected QT interval (QTc, Bazett's formula) was>500ms and the risk-benefit ratio of HCQ+AZ treatment was estimated by the infectious disease specialist and agreed with the cardiologist, to be between 460 and 500ms. The indications for this control ECG were restricted after an initial workup in 848 ECG from 424 patients (at day 0 and day 2 for each patient), showing that all contraindicative repolarization abnormalities had been detected on the first ECG [2]. Among 3,737 COVID-19 patients diagnosed at our institute in March-April 2020, 88 (2.4%) had cardiac contraindications to combination therapy, 45 (1.2%) patients were taking a drug with a potential risk of interactions with combination therapy and 10 (0.3%) had hypo or hyperkalaemia [3]. A total of 3,119 patients received HCQ-AZ for at least three days. QTc prolongation (>60 ms) was observed in 25 patients (0.67%), resulting in discontinuation of treatment in 12 cases, including three cases with QTc> 500 ms. No cases of torsade de pointe or sudden death were observed, including in the 9.5% of patients over 65 years of age.

Our current observations and practices illustrate the efficacy of this risk management procedures associated with the prescription of HCQ-AZ, which presents an excellent safety profile in COVID-19 patients, including elderly patients [4].

We agree that doxycycline has shown *in vitro* effect on SARS-CoV-2 [5]. However, synergistic between doxycycline and hydroxychloroquine *in vitro* effect has not been investigated so far, unlike azithromycin. Therefore, the combination of HCQ and doxycycline should only be proposed for patients with a contraindication to the HCQ-AZ regimen, independently of age.

Declaration of Competing Interest

The authors declare no competing interests.

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Ethical approval

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